



OCKET NO.: MOR-0241/HD0002US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Luigi Grasso, et al.

Application No.: 10/624,631

Filing Date: July 21, 2003

Confirmation No.: Not Yet Assigned

Group Art Unit: Not Yet Assigned

Examiner: Not Yet Assigned

**For: METHODS FOR GENERATING ENHANCED ANTIBODY-PRODUCING
CELL LINES WITH IMPROVED GROWTH CHARACTERISTICS**

DATE OF DEPOSIT: *October 3, 2003*

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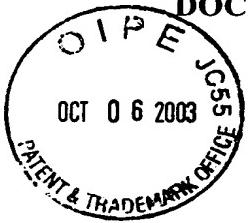
Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).

- In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in § 1.491, before the mailing date



of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

- In accordance with § 1.129(a), this Information Disclosure Statement is being filed in connection with the first or second After Final Submission, therefore:
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- Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.



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EXCEPT THAT:

In view of the voluminous nature of references 1,17, 24 and 41 and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.

In accordance with § 1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. § 120 have been made in the instant application:

Copies of references [list as appropriate] listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior Application No.

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OCT 06 2003

The relevance of those listed references which are not in the English language is as follows:

- There are no listed references which are not in the English language.

Date: October 3, 2003


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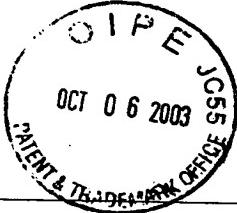
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|---|----|---|
| * | 1 | Ausubel, et al., Current Protocols in Molecular Biology, <i>John Wiley & Sons, New York, 1998</i> |
| | 2 | Baker, S.M., et al., "Male defective in the DNA mismatch repair gene PMS2 exhibit abnormal chromosome synapsis in meiosis," <i>Cell</i> , July 28, 1995, 82, 309-319 |
| | 3 | Barr, P.J., et al., "Active site modified protease .alpha.-1-antitrypsin inhibitors, Patent: US 4,732,973 A, March 22, 1988, Chiron corp., Emeryville, CA, GenBank Accession No. I00556, 2 pages |
| | 4 | Bignami, M., "Unmasking a killer: DNA O ⁶ -methylguanine and the cytotoxicity of methylating agents," <i>Mutat. Res.</i> , 2000, 462, 71-82 |
| | 5 | Bocker, T., et al., "hMSH5: a human MutS homologue that forms a novel heterodimer with hMSH4 and is expressed during spermatogenesis," <i>Cancer Res.</i> , February 15, 1999, 59, 816-822 |
| | 6 | Bronner, C.E., et al., "Mutation in the DNA mismatch repair gene homologue <i>hMLH1</i> is associated with hereditary non-polyposis colon cancer," <i>Nature</i> , 1994, 368, 258-261 |
| | 7 | deWind, N., et al., "Inactivation of the mouse <i>Msh2</i> gene results in mismatch repair deficiency, methylation tolerance, hyperrecombination, and predisposition to cancer," <i>Cell</i> , July 28, 1995, 82, 321-330 |
| | 8 | Drummond, J.T., et al., "Isolation of an hMSH2-p160 heterodimer that restores mismatch repair to tumor cells," <i>Science</i> , June 30, 1995, 268, 1909-1912 |
| | 9 | Drummond, J.T., et al., "Cisplatin and adriamycin resistance are associated with MutL α and mismatch repair deficiency in an ovarian tumor cell line," <i>J. Biol. Chem.</i> , August 16, 1996, 271(33), 19645-19648 |
| | 10 | Emery, S.C., et al., "Strategies for humanizing antibodies," In: Antibody Engineering C.A.K., Borrebaeck (Ed.), <i>Oxford University Press, NY, 1995</i> , 159-183 |

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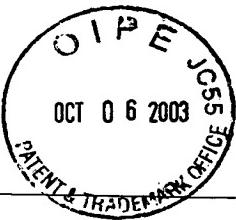
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| | |
|----|--|
| 11 | Eshleman, J.R., et al., "Mismatch repair defects in human carcinogenesis," <i>Hum. Mol. Genet.</i> , 1996, 5, 1489-1494 |
| 12 | Fan, Y., et al., "Endothelial-monocyte activating polypeptide (EMAP) I/S100C: A tumor-derived cytokine which activates host response mechanisms," <i>Unpublished</i> , GenBank Accession No. MMU41341, 2 pages |
| 13 | Fiedler, U., et al., "High-level production and long-term storage of engineered antibodies in transgenic tobacco seeds," <i>Bio/Technology</i> , October 1995, 13, 1090-1093 |
| 14 | Frigerio, L., et al., "Assembly, secretion, and vacuolar delivery of a hybrid immunoglobulin in plants," <i>Plant Physiol.</i> , August 2000, 123, 1483-1494 |
| 15 | Galio, L., et al., "ATP hydrolysis-dependent formation of a dynamic ternary nucleoprotein complex with MutS and MutL," <i>Nucl. Acids Res.</i> , 1999, 27(11), 2325-2331 |
| 16 | Glaser, V., "Can ReoPro repolish tarnished monoclonal therapeutics?," <i>Nat. Biotechnol.</i> , October 1996, 14, 1216-1217 |
| * | Kaufman, M.B., et al., Handbook of Molecular and Cellular Methods in Biology and Medicine, <i>CRC Press, Boca Raton</i> , 1995 |
| 18 | Khazaeli, M.B., et al., "Human immune response to monoclonal antibodies," <i>J. Immunother.</i> , 1994, 15, 42-52 |
| 19 | Koi, M., et al., "Human chromosome 3 corrects mismatch repair deficiency and microsatellite instability and reduces N-methyl-N'-nitro-N-nitrosoguanidine tolerance in colon tumor cells with homozygous hMLH1 mutation," <i>Cancer Res.</i> , August 15, 1994, 15, 4308-4312 |
| 20 | Lawson, W.B., et al., "Studies on the inhibition of human thrombin: effects of plasma and plasma constituents," <i>Folia Haematol.</i> , 1982, 109(1S), 52-60 |

EXAMINER**DATE CONSIDERED**

* A copy of this reference will not be forwarded to the U.S. Patent and Trademark Office since it is believed to be too voluminous and easily obtainable by the Examiner.



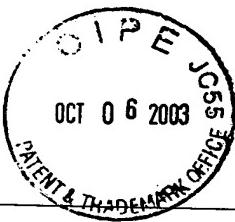
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|---|--------------------------------------|-------------------------------|
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| | Confirmation No. Not Yet Assigned | |

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|---|-----------|---|
| | 21 | Lindor, N.M., et al., "Search for chromosome instability in lymphocytes with germ-line mutations in DNA mismatch repair genes," <i>Cancer Genet Cytogenet</i> , 1998 , <i>104</i> , 48-51 |
| | 22 | Lipkin, S.M., et al., MLH3: a DNA mismatch repair gene associated with mammalian microsatellite instability," <i>Nat. Genet.</i> , January 2000 , <i>24</i> , 27-35 |
| | 23 | Liu, T., et al., "Microsatellite instability as a predictor of a mutation in a DNA mismatch repair gene in familial colorectal cancer," <i>Genes Chromosomes Cancer</i> , 2000 , <i>27</i> , 17-25 |
| * | 24 | McPherson (Ed.), Directed Mutagenesis: A Practical Approach, <i>IRL Press, Oxford</i> , 1991 |
| | 25 | Modrich, P., "Mismatch repair, genetic stability, and cancer," <i>Science</i> , December 23, 1994 , <i>266</i> , 1959-1960 |
| | 26 | Müller, A., et al., "Mismatch repair and the hereditary non-polyposis colorectal cancer syndrome (HNPCC)," <i>Cancer Invest.</i> , 2002 , <i>20</i> (1), 102-109 |
| | 27 | Neuberger, M., et al., "Monoclonal antibodies: mice perform a human repertoire," <i>Nature</i> , March 6, 1997 , <i>386</i> , 25-26 |
| | 28 | Nicolaides, N.C., et al., "A naturally occurring hPMS2 mutation can confer a dominant negative mutator phenotype," <i>Mol. Cell. Biol.</i> , March 1998 , <i>18</i> (3), 1635-1641 |
| | 29 | Nicolaides, N.C., et al., "Analysis of the 5' region of PMS2 reveals heterogenous transcripts and a novel overlapping gene," <i>Genomics</i> , 1995 , <i>29</i> , 329-334 |
| | 30 | Nicolaides, N.C., et al., "Genomic organization of the human PMS2 gene family," <i>Genomics</i> , 1995 , <i>30</i> , 195-206 |

EXAMINER**DATE CONSIDERED**

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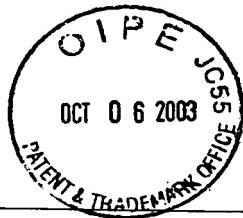
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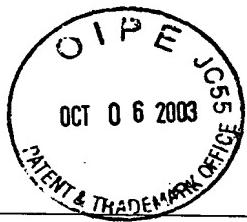
| | |
|----|---|
| 31 | Nicolaides, N.C., et al., "The Jun family members, c-JUN and JUND, transactivate the human <i>c-myb</i> promoter via an Ap1 like element," <i>J. Biol. Chem.</i> , September 25, 1992, 267(27), 19665-19672 |
| 32 | Nicolaides, N.C., et al., "Interleukin 9: A candidate gene for asthma," <i>Proc. Natl. Acad. Sci. USA</i> , November 1997, 94, 13175-13180 |
| 33 | Palombo, F., et al., "Mismatch repair and cancer," <i>Nature</i> , February 1994, 36, 417 |
| 34 | Parsons, R., et al., "Hypermutability and mismatch repair deficiency in RER+ tumor cells," <i>Cell</i> , December 17, 1993, 75, 1227-1236 |
| 35 | Papadopoulos, N., et al., "Mutation of a mutL homolog is associated with hereditary colon cancer," <i>Science</i> , 1993, 263, 1625-1629 |
| 36 | Perucho, M., "Cancer of the microsatellite mutator phenotype," <i>Biol. Chem.</i> , November 1996, 377, 675-684 |
| 37 | Prolla, T.A., et al., "MLH1, PMS1, and MSH2 interaction during the initiation of DNA mismatch repair in yeast," <i>Science</i> , August 19, 1994, 264, 1091-1093 |
| 38 | Qian, Y., et al., "Molecular events after antisense inhibition of hMSH2 in a HeLa cell line," <i>Mutat Res.</i> , 1998, 418, 61-71 |
| 39 | Reff, M.E., "High-level production of recombinant immunoglobulins in mammalian cells," <i>Curr. Opin. Biotechnol.</i> , 1993, 4, 573-576 |
| 40 | Saez-Llorens, X.E., et al., "Safety and pharmacokinetics of an intramuscular humanized monoclonal antibody to respiratory syncytial virus in premature infants and infants with bronchopulmonary dysplasia," <i>Pediat. Infect. Dis. J.</i> , 1998, 17, 787-791 |

EXAMINER**DATE CONSIDERED**



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| Form PTO-1449 Modified | | Docket No. MOR-0241/ HD0002US | Application No. 10/624,631 |
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| | | Confirmation No. Not Yet Assigned | |
| OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) | | | |
| * | 41 | Sambrook, et al., Molecular Cloning: A Laboratory Manual, 2 nd Ed. <i>Cold Spring Harbor Laboratory Press, Plainview, NY, 1989</i> | |
| | 42 | Shield, C.F., et al., "A cost-effective analysis of OKT3 induction therapy in cadaveric kidney transplantation," <i>Am. J. Kidney Dis.</i> , June 1996 , 27(6), 855-864 | |
| | 43 | Shields, R.L., et al., "Anti-IgE monoclonal antibodies that inhibit allergen-specific histamine release," <i>Int. Arch. Allergy Immunol.</i> , 1995 , 107, 412-413 | |
| | 44 | Strand, M., et al., "Destabilization of tracts of simple repetitive DNA in yeast by mutations affecting DNA mismatch repair," <i>Nature</i> , September 16, 1993 , 365, 274-276 | |
| | 45 | Su, S.-S., et al., "Mispair specificity of methyl directed DNA mismatch corrections in vitro," <i>J. Biol. Chem.</i> , May 15, 1988 , 263(14), 6829-6835 | |
| | 46 | Weiner, L.M., "Monoclonal antibody therapy of cancer," <i>Semin. In Oncol.</i> , October 1999 , 26(5), Suppl. 14, 43-51 | |
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| | |
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U. S. PATENT DOCUMENTS

| Examiner Initial | | Document No. | Date | Name | Class | Subclass |
|------------------|----|--------------|----------|--------------------|-------|----------|
| | 47 | 4,732,973 | 03/22/88 | Barr, et al. | 530 | 350 |
| | 48 | 5,530,101 | 06/25/96 | Queen, et al. | 530 | 387.3 |
| | 49 | 6,146,894 | 11/14/00 | Nicolaides, et al. | 435 | 440 |
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FOREIGN PATENT DOCUMENTS

| Examiner Initial | | Document No. | Date | Country | Translation | |
|------------------|----|--------------|----------|---------|-------------|----|
| | | | | | YES | NO |
| | 50 | WO 02/054856 | 07/18/02 | PCT | | |
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